IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appln. No. : 09/806,370 Confirmation No.: 8568

Appellant : Holmes et al.

Filed : October 3, 2001

TC/A.U. : 1645

Examiner : V. Portner

Docket No. : 33,383-00

Customer No. : 38199

VIA FACSIMILE to Examiner Portner (571-273-0862)

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22323-1450

STATEMENT OF THE SUBSTANCE OF THE INTERVIEW

Sir:

Applicants and the undersigned express their appreciation to Examiner Portner for the courtesy of the telephone conference with Robert J. Duminiak (Reg. No. 51,636) on February 12, 2008. This telephone conference was initiated by Examiner Portner and was responsive to our telephonic inquiry for the status of the application following the Decision on Appeal dated December 11, 2007.

The recordation of the substance of the interview is provided by the following Proposed Examiner's Amendments and the remarks herein. Examiner Portner indicated her willingness to allow claims 4-11, 14-17, 28-37 and 39-42, which were objected to within the Examiner's Answer (mailed January 17, 2007) as dependent upon a rejected base claim. Robert Duminiak indicated to Examiner Portner that, in

addition to the objected to claims, claims 3, 43 and 44 were allowed, as indicated in the Examiner's Answer.

Examiner Portner requested that Applicants provide a Proposed Examiner's Amendment, containing amendments to the objected to claims placing them in allowable form, and cancelling all rejected claims. Applicants believe that the amendments marked-up in the in the attached claim set are reflective of agreement reached.

The Examiner is respectfully requested to consider and enter the attached amendments via Examiner's Amendment.

While no fee is believed due, the Director is hereby authorized to charge any deficiency in any fees due with the filing of this paper, or credit any overpayment, to our deposit account, Number 08-3040.

Respectfully submitted,

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Proposed Examiner's Amendment of Claims

Claims 1-2 (Canceled).

Claim 3 (Previously Presented): An antigenic composition comprising

(a) at least one antigen from a pathogenic organism selected from the group consisting of a bacterium, a virus, a fungus and a parasite; and

(b) an effective adjuvanting amount of a mutant cholera holotoxin, wherein the mutant holotoxin has reduced toxicity compared to wild-type cholera holotoxin, and has a histidine which replaces the glutamic acid which naturally occurs at position 29 of the A subunit of the wild-type cholera holotoxin and wherein said mutant holotoxin enhances the immune response in a vertebrate host to said antigen.

Claim 4 (Currently Amended): [[The]] An antigenic composition ~~of Claim 1 wherein the~~ comprising

(a) at least one antigen [[[is]] selected from the group consisting of the *Haemophilus influenzae* P4 outer membrane protein, the *Haemophilus influenzae* P6 outer membrane protein, the *Haemophilus influenzae* adherence and penetration protein (Hap_s), the *Helicobacter pylori* urease protein, the *Neisseria meningitidis* Group B recombinant class 1 pilin (rpilin), the *Neisseria meningitidis* Group B class 1 outer membrane protein (PorA), the respiratory syncytial virus fusion protein, a rotavirus virus-like particle and the herpes simplex virus (HSV) type 2 glycoprotein D (gD2); and

(b) an effective adjuvanting amount of a mutant cholera holotoxin, wherein the mutant holotoxin has reduced toxicity compared to a wild-type cholera holotoxin, and has an amino acid which replaces the deleted glutamic acid which naturally occurs at position 29 of the mature A subunit of the wild-type cholera

holotoxin, wherein said amino acid is other than aspartic acid, and wherein said mutant holotoxin enhances the immune response in a vertebrate host to said antigen.

Claim 5 (Previously Presented): The antigenic composition of Claim 4 wherein the antigen is selected from the group consisting of the *Haemophilus influenzae* P4 outer membrane protein, the *Haemophilus influenzae* P6 outer membrane protein, the *Haemophilus influenzae* Hap_s protein, and any combination thereof.

Claim 6 (Previously Presented): The antigenic composition of Claim 4 wherein the antigen is the *Helicobacter pylori* urease protein.

Claim 7 (Previously Presented): The antigenic composition of Claim 4 the antigen is selected from the group consisting of the *Neisseria meningitidis* rpilin, *Neisseria meningitidis* PorA protein and any combination thereof.

Claim 8 (Previously Presented): The antigenic composition of Claim 4 wherein the antigen is the respiratory syncytial virus fusion protein.

Claim 9 (Previously Presented): The antigenic composition of Claim 4 wherein the antigen is a rotavirus virus-like particle.

Claim 10 (Original): The antigenic composition of Claim 9 wherein the virus-like particle is a rotavirus 2/6-virus-like particle.

Claim 11 (Previously Presented): The antigenic composition of Claim 4 wherein the antigen is HSV gD2.

Claims 12-13 (Canceled).

Claim 14 (Currently Amended): [[The]] An antigenic composition ~~of Claim 1 which further comprises~~ comprising

(a) at least one antigen from a pathogenic organism selected from the group consisting of a bacterium, a virus, a fungus and a parasite;

(b) an effective adjuvanting amount of a mutant cholera holotoxin, wherein the mutant holotoxin has reduced toxicity compared to a wild-type cholera holotoxin, and has an amino acid which replaces the deleted glutamic acid which naturally occurs at position 29 of the mature A subunit of the wild-type cholera holotoxin, wherein said amino acid is other than aspartic acid, and wherein said mutant holotoxin enhances the immune response in a vertebrate host to said antigen; and

(c) a second adjuvant in addition to the mutant cholera holotoxin.

Claim 15 (Currently Amended): [[The]] An antigenic composition ~~of Claim 1, wherein~~ comprising

(a) at least one antigen from a pathogenic organism selected from the group consisting of a bacterium, a virus, a fungus and a parasite;

(b) an effective adjuvanting amount of a mutant cholera holotoxin, wherein the mutant holotoxin has reduced toxicity compared to a wild-type cholera holotoxin, and has an amino acid which replaces the deleted glutamic acid which naturally occurs at position 29 of the mature A subunit of the wild-type cholera holotoxin, wherein said amino acid is other than aspartic acid, and wherein said mutant holotoxin enhances the immune response in a vertebrate host to said antigen; and

(c) at least one additional mutation ~~is made to~~ in the A subunit of the mutant cholera holotoxin at a position other than said wild-type amino acid position 29.

Claim 16 (Previously Presented): The antigenic composition of Claim 15 wherein the at least one additional mutation is made as a substitution for a naturally-occurring amino acid at an amino acid position of wild-type cholera holotoxin selected from the group consisting of the arginine at amino acid 7, the aspartic acid at position 9, the arginine at position 11, the histidine at position 44, the valine at position 53, the arginine at position 54, the serine at position 61, the serine at position 63, the histidine at position 70, the valine at position 97, the tyrosine at position 104, the proline at position 106, the histidine at position 107, the serine at position 109, the glutamic acid at position 100, the glutamic acid at position 112, the serine at position 114, the tryptophan at position 127, the arginine at position 146 and the arginine at position 192.

Claim 17 (Currently Amended): A method for increasing the ability of an antigenic composition containing at least one antigen from a pathogenic organism selected from the group consisting of a bacterium, a virus, a fungus or a parasite to elicit the immune response of a vertebrate host, which comprises administering to said host an antigenic composition [[of Claim 1]] comprising

(a) at least one antigen from a pathogenic organism selected from the group consisting of a bacterium, a virus, a fungus and a parasite; and

(b) an effective adjuvanting amount of a mutant cholera holotoxin, wherein the mutant holotoxin has reduced toxicity compared to a wild-type cholera holotoxin, and has an amino acid which replaces the deleted glutamic acid which naturally occurs at position 29 of the mature A subunit of the wild-type cholera holotoxin, wherein said amino acid is other than aspartic acid, and wherein said mutant holotoxin enhances the immune response in a vertebrate host to said antigen.

Claims 18-27 (Canceled).

Claim 28 (Previously Presented): The method of Claim 17 wherein the antigenic composition comprises more than one antigen.

Claim 29 (Previously Presented): The method of Claim 17 wherein the amino acid substituted at wild-type position 29 is histidine.

Claim 30 (Previously Presented): The method of Claim 17 wherein the antigen is selected from the group consisting of the *Haemophilus influenzae* P4 outer membrane protein, the *Haemophilus influenzae* P6 outer membrane protein, the *Haemophilus influenzae* Hap_s protein, the *Helicobacter pylori* urease protein, the *Neisseria meningitidis* rpilin, the *Neisseria meningitidis* PorA protein, the respiratory syncytial virus fusion protein, a rotavirus, virus-like particle and HSV gD2.

Claim 31 (Previously Presented): The method of Claim 30 wherein at least one antigen is selected from the group consisting of the *Haemophilus influenzae* P4 outer membrane protein, the *Haemophilus influenzae* P6 outer membrane protein, the *Haemophilus influenzae* Hap_s protein, and any combination thereof.

Claim 32 (Previously Presented): The method of Claim 30 wherein the antigen is the *Helicobacter pylori* urease protein.

Claim 33 (Previously Presented): The method of Claim 30 wherein at least one antigen is selected from the group consisting of the *Neisseria meningitidis* rpilin, *Neisseria meningitidis* PorA protein and any combination thereof.

Claim 34(Previously Presented): The method of Claim 30 wherein the antigen is the respiratory syncytial virus fusion protein.

Claim 35 (Previously Presented): The method of Claim 30 wherein the antigen is a rotavirus virus-like particle.

Claim 36 (Original): The method of Claim 35 wherein the virus-like particle is a rotavirus 2/6-virus-like particle.

Claim 37 (Previously Presented): The method of Claim 30 wherein the antigen is HSV gD2.

Claim 38 (Canceled).

Claim 39 (Original): The method of Claim 17 wherein the antigenic composition further comprises a diluent or carrier.

Claim 40(Original): The method of Claim 17 wherein the antigenic composition further comprises a second adjuvant in addition to the mutant cholera holotoxin.

Claim 41 (Previously Presented): The method of Claim 17 wherein at least one additional mutation is made to the A subunit of the mutant cholera holotoxin at a position other than said wild-type amino acid position 29, wherein said mutant holotoxin with said additional mutation enhances the immune response in a vertebrate host to said antigen.

Claim 42 (Previously Presented): The method of Claim 41 wherein the at least one additional mutation is made as a substitution for a naturally-occurring amino acid of wild-type cholera holotoxin selected from the group consisting of the arginine at amino acid 7, the aspartic acid at position 9, the arginine at position 11, the histidine

at position 44, the valine at position 53, the arginine at position 54, the serine at position 61, the serine at position 63, the histidine at position 70, the valine at position 97, the tyrosine at position 104, the proline at position 106, the histidine at position 107, the serine at position 109, the glutamic acid at position 100, the glutamic acid at position 112, the serine at position 114, the tryptophan at position 127, the arginine at position 146 and the arginine at position 192.

Claim 43 (Previously Presented): A method of preparing an antigenic composition comprising combining

(a) at least one antigen from a pathogenic organism selected from the group consisting of a bacterium, a virus, a fungus and a parasite; and

(b) an effective adjuvanting amount of a mutant cholera holotoxin, wherein the mutant holotoxin has reduced toxicity compared to wild-type cholera holotoxin and has a substitution which replaces the glutamic acid which naturally occurs at position 29 of the A subunit of the wild-type cholera holotoxin with an amino acid other than aspartic acid, and wherein said mutant holotoxin enhances the immune response in a vertebrate host to said antigen.

Claim 44 (Previously Presented): A method for increasing the ability of an antigenic composition containing at least one antigen from a pathogenic organism selected from the group consisting of a bacterium, a virus, a fungus or a parasite to elicit the immune response of a vertebrate host, which comprises administering to said host an antigenic composition of Claim 3.